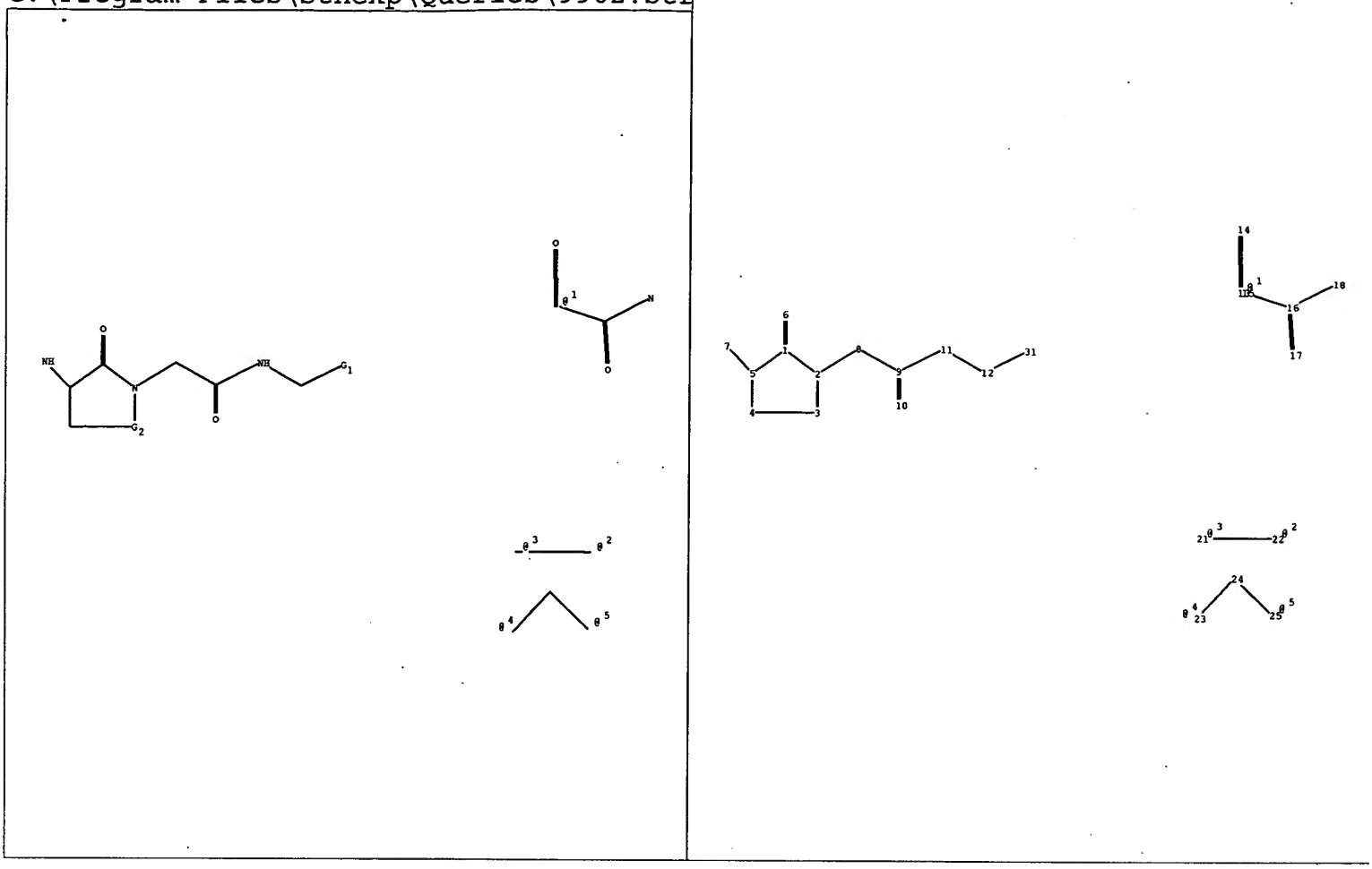
C:\Program Files\Stnexp\Queries\9902.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 21 22 23 24 25 31
ring nodes :
1 2 3 4 5
chain bonds :
1-6 2-8 5-7 8-9 9-10 9-11 11-12 12-31 13-14 15-16 16-17 16-18
21-22 23-24 24-25
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-6 2-3 2-8 3-4 4-5 5-7 8-9 9-10 9-11 11-12 12-31
13-14 15-16 16-17 16-18 21-22 23-24 24-25

G1:B,[*1]

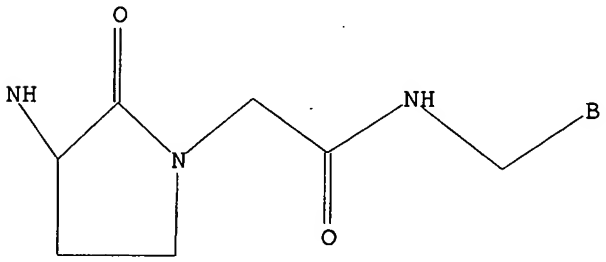
G2:[*2-*3],[*4-*5]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS
16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
25:CLASS 31:CLASS

=> d que stat
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L5 72 SEA FILE=REGISTRY SSS FUL L3
L8 STR



G1

G2

Structure attributes must be viewed using STN Express query preparation.
L10 9 SEA FILE=REGISTRY SSS FUL L8
L12 7 SEA FILE=HCAPLUS (L5 OR L10) AND (CANCER? OR NEOPLAS? OR LEUKEM? OR MYELOM? OR CARCINOM? OR ADENOCARCINOM? OR TUMOR? OR TUMOUR? OR PROTEASOM?(3A)INHIBITOR? OR PROTEASOM?(3A)ANTAGONIST ? OR THREONIN?(3A)PROTEAS?(3A)INHIBIT?)

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=> d his full

     (FILE 'HOME' ENTERED AT 21:47:06 ON 02 OCT 2005)

     FILE 'REGISTRY' ENTERED AT 21:47:16 ON 02 OCT 2005
L1                STRUCTURE UPLOADED
                  D L1
L2              1 SEA SSS SAM L1
                  D SCAN L2

     FILE 'STNGUIDE' ENTERED AT 21:48:20 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:51:45 ON 02 OCT 2005
L3                STRUCTURE UPLOADED
                  D L3
L4              1 SEA SSS SAM L3
                  D SCAN L4
L5             72 SEA SSS FUL L3

     FILE 'STNGUIDE' ENTERED AT 21:53:06 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:54:22 ON 02 OCT 2005
L6                STRUCTURE UPLOADED
                  D L6
L7              0 SEA SSS SAM L6
L8                STRUCTURE UPLOADED
                  D L8
L9              0 SEA SSS SAM L8
L10             9 SEA SSS FUL L8
                  D SCAN L10

     FILE 'STNGUIDE' ENTERED AT 21:56:45 ON 02 OCT 2005

     FILE 'HCAPLUS' ENTERED AT 21:58:16 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:58:49 ON 02 OCT 2005
L11             0 SEA SSS FUL L6
                  D HCAPLUS

     FILE 'HCAPLUS' ENTERED AT 21:59:04 ON 02 OCT 2005
L12             7 SEA (L5 OR L10 ) AND (CANCER? OR NEOPLAS? OR LEUKEM? OR
                  MYELOM? OR CARCINOM? OR ADENOCARCINOM? OR TUMOR? OR TUMOUR? OR
                  PROTEASOM?(3A)INHIBITOR? OR PROTEASOM?(3A)ANTAGONIST? OR
                  THREONIN?(3A)PROTEAS?(3A)INHIBIT?)
                  D L12 ABS CBIB KWIC HITSTR 1-7

     FILE 'STNGUIDE' ENTERED AT 22:01:37 ON 02 OCT 2005
                  D QUE STAT


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.
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STRUCTURE FILE UPDATES: 30 SEP 2005 HIGHEST RN 864353-93-5
DICTIONARY FILE UPDATES: 30 SEP 2005 HIGHEST RN 864353-93-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 30, 2005 (20050930/UP).

FILE HCAPLUS

FILE COVERS 1907 - 2 Oct 2005 VOL 143 ISS 15
FILE LAST UPDATED: 30 Sep 2005 (20050930/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

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=> d his

     (FILE 'HOME' ENTERED AT 21:47:06 ON 02 OCT 2005)

     FILE 'REGISTRY' ENTERED AT 21:47:16 ON 02 OCT 2005
L1             STRUCTURE UPLOADED
L2           1 S L1 SSS SAM

     FILE 'STNGUIDE' ENTERED AT 21:48:20 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:51:45 ON 02 OCT 2005
L3             STRUCTURE UPLOADED
L4           1 S L3 SSS SAM
L5          72 S L3 SSS FULL

     FILE 'STNGUIDE' ENTERED AT 21:53:06 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:54:22 ON 02 OCT 2005
L6             STRUCTURE UPLOADED
L7           0 S L6 SSS SAM
L8             STRUCTURE UPLOADED
L9           0 S L8 SSS SAM
L10          9 S L8 SSS FULL

     FILE 'STNGUIDE' ENTERED AT 21:56:45 ON 02 OCT 2005

     FILE 'HCAPLUS' ENTERED AT 21:58:16 ON 02 OCT 2005

     FILE 'REGISTRY' ENTERED AT 21:58:49 ON 02 OCT 2005
L11          0 S L6 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 21:59:04 ON 02 OCT 2005

=> s (l5 or l10 ) and (cancer? or neoplas? or leukem? or myelom? or carcinom? or
adenocarcinom? or tumor? or tumour? or proteasom?(3a)inhibitor? or
proteasom?(3a)antagonist? or threonin?(3a)proteas?(3a)inhibit?)
           35 L5
            4 L10
       270874 CANCER?
       423952 NEOPLAS?
        97415 LEUKEM?
        19465 MYELOM?
       141608 CARCINOM?
        27550 ADENOCARCINOM?
       403927 TUMOR?
         3382 TUMOUR?
        10310 PROTEASOM?
       949701 INHIBITOR?
         2847 PROTEASOM?(3A)INHIBITOR?
        10310 PROTEASOM?
       225248 ANTAGONIST?
           12 PROTEASOM?(3A)ANTAGONIST?
        54530 THREONIN?
       113547 PROTEAS?
      1774511 INHIBIT?
           13 THREONIN?(3A)PROTEAS?(3A)INHIBIT?
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L12 7 (L5 OR L10) AND (CANCER? OR NEOPLAS? OR LEUKEM? OR MYELOM? OR CARCINOM? OR ADENOCARCINOM? OR TUMOR? OR TUMOUR? OR PROTEASOM?(3A)INHIBITOR? OR PROTEASOM?(3A)ANTAGONIST? OR THREONIN?(3A)PROTEAS?(3A)INHIBIT?)

=> d l12 abs cbib kwic hitstr 1-7

L12 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The present invention is directed to compns. of matter useful for the enhancement of apoptosis in mammals and to methods of using those compns. of matter for the same. BDB (BIR domain-binding) oligopeptides that specifically bind to ML-IAP (melanoma inhibitor of apoptosis) and release the inhibitory effect ML-IAP has on caspase activity are claimed. Apoptosis in **cancer** cells is increased by administering the oligopeptide.

2004:702118 Document Number 141:218943 Compositions and methods for enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase. Fairbrother, Wayne J.; Deshayes, Kurt; Fischer, Saloumeh; Flygare, John A.; Franklin, Matthew C.; Vucic, Domagoj (Genentech, Inc., USA). PCT Int. Appl. WO 2004072641 A1 20040826, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US3799 20030207.

AB . . . to ML-IAP (melanoma inhibitor of apoptosis) and release the inhibitory effect ML-IAP has on caspase activity are claimed. Apoptosis in **cancer** cells is increased by administering the oligopeptide.

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRAIL (**tumor** necrosis factor-related apoptosis-inducing ligand); enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT Diagnosis
(**cancer**; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT Nervous system, **neoplasm**
(central; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT Uterus, **neoplasm**
(cervix; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT Intestine, **neoplasm**
(colorectal; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT Antitumor agents
Apoptosis
Bladder, **neoplasm**
Combination chemotherapy
Drug delivery systems
Human

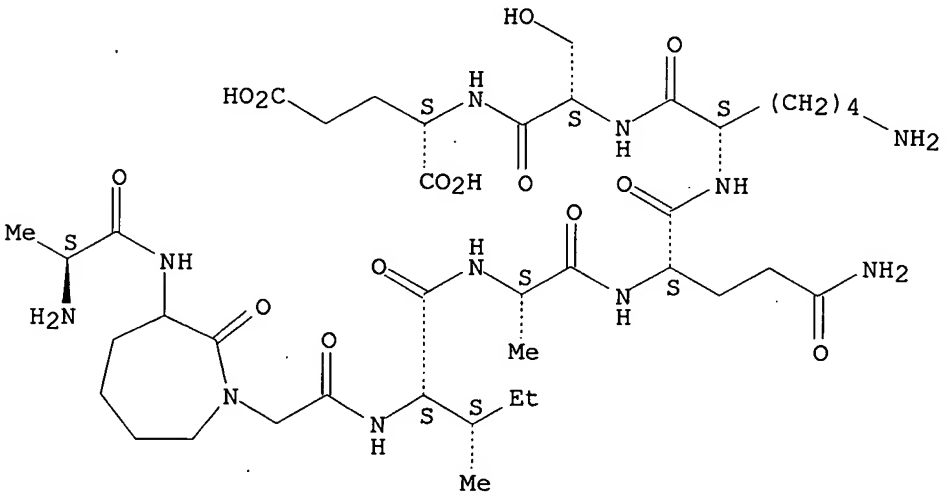
Leukemia
Liver, **neoplasm**
Lung, **neoplasm**
Mammalia
Mammary gland, **neoplasm**
Melanoma
Neoplasm
Ovary, **neoplasm**
Pancreas, **neoplasm**
Phage display library
(enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

IT 744199-35-7P 744199-69-7P 744199-70-0P 744199-71-1P 744199-72-2P
744199-73-3P 744199-74-4P 744199-75-5P 744199-76-6P 744199-77-7P
744199-78-8P 744199-79-9P 744199-80-2P 744199-81-3P 744199-82-4P
744199-84-6P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(response to BIR domains; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

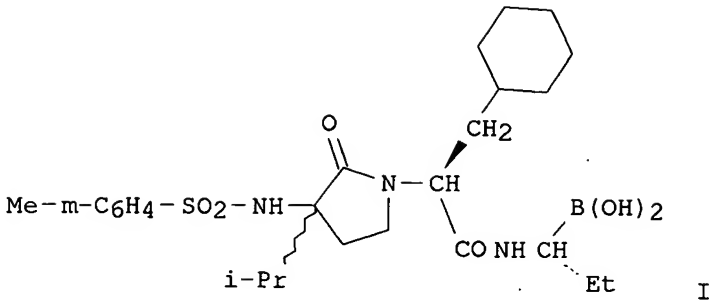
IT **744199-84-6P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(response to BIR domains; enhancing apoptosis using BIR domain-binding oligopeptides to release melanoma inhibitor of apoptosis protein from caspase)

RN 744199-84-6 HCAPLUS
CN L-Glutamic acid, L-alanyl-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-L-isoleucyl-L-alanyl-L-glutaminyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



I

AB Synthesis and in vitro characterization of a novel, lactam boronic acid based, selective, and rapidly reversible inhibitor, e.g., I, of the 20S-proteasome is presented.

2004:689253 Document Number 141:366258 Identification of a potent and rapidly reversible **inhibitor** of the 20S-**proteasome**. Purandare, Ashok V.; Wan, Honghe; Laing, Naomi; Benbatoul, Khalid; Vaccaro, Wayne; Poss, Michael A. (Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA). Bioorganic & Medicinal Chemistry Letters, 14(18), 4701-4704 (English) 2004. CODEN: BMCLE8. ISSN: 0960-894X. OTHER SOURCES: CASREACT 141:366258. Publisher: Elsevier B.V..

TI Identification of a potent and rapidly reversible **inhibitor** of the 20S-**proteasome**

ST lactam boronic acid prepn **inhibitor proteasome** enzyme

IT Acids, preparation
Group IIIA element compounds
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(boronic acids; preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT Enzymes, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors; preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT Lactams
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT **323196-93-6**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT **779357-81-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT **779357-87-8 779357-89-0 779357-91-4**
779357-93-6 779357-95-8 779357-97-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT 106-95-6, Allyl bromide, reactions 121-43-7, Trimethyl borate
925-90-6, Ethylmagnesium bromide 926-62-5, Isobutylmagnesium bromide
1149-26-4 1899-93-0 5419-55-6, Triisopropyl borate 18680-27-8
30525-89-4, Paraformaldehyde 40056-18-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT 85167-14-2P 87249-60-3P 98541-37-8P 178455-04-4P 319009-92-2P
319010-99-6P 323197-10-0P 323197-12-2P 323197-13-3P 779357-79-8P
779357-80-1P 779357-85-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT 4039-32-1, (Hexamethyldisilazane)lithium
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

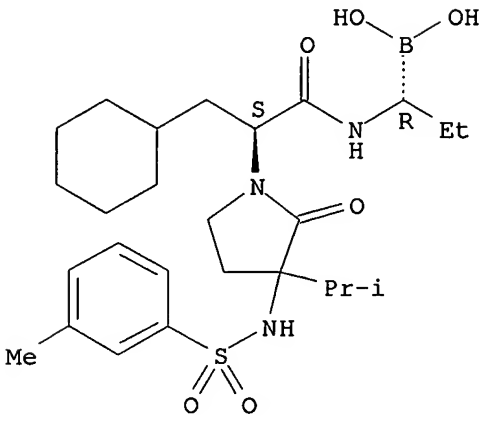
IT **779357-83-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT 779357-78-7P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and resolution in the preparation and in vitro characterization of
lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

IT **323196-93-6**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

RN 323196-93-6 HCAPLUS
CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

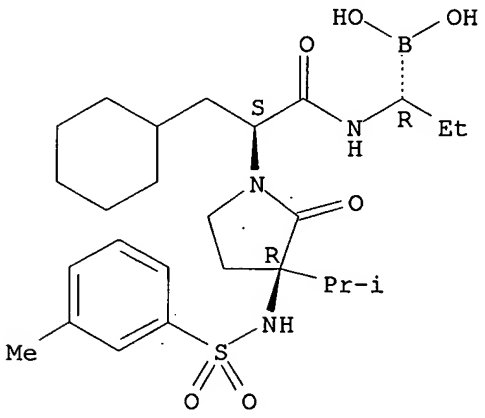


IT **779357-81-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

RN 779357-81-2 HCAPLUS

CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[(3R)-3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

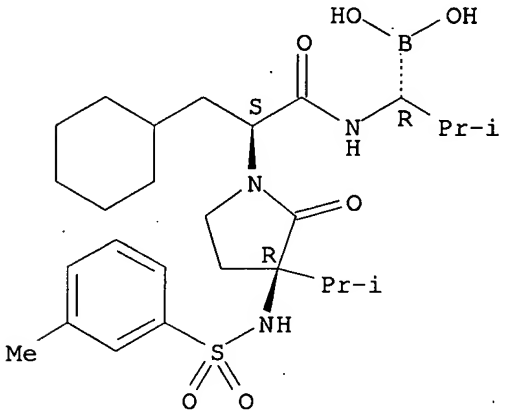


IT **779357-87-8 779357-89-0 779357-91-4**
779357-93-6 779357-95-8 779357-97-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)

DELACROIX

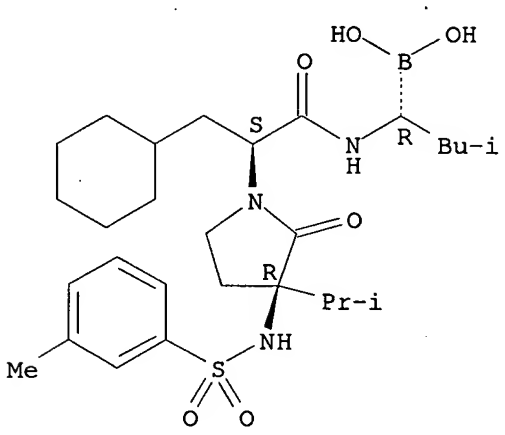
RN 779357-87-8 HCAPLUS
CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[(3R)-3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



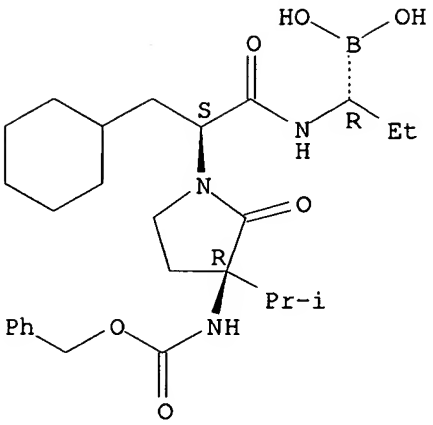
RN 779357-89-0 HCAPLUS
CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[(3R)-3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



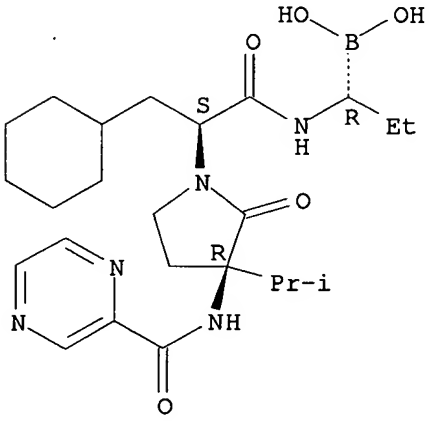
RN 779357-91-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[(1S)-2-[[(1R)-1-boronopropyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]-3-(1-methylethyl)-2-oxo-3-pyrrolidinyl]-, C-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



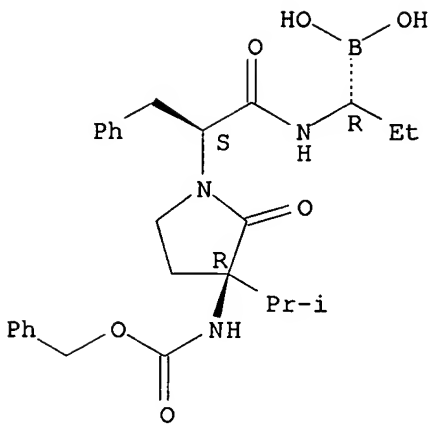
RN 779357-93-6 HCAPLUS
CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[(3R)-3-(1-methylethyl)-2-oxo-3-[(pyrazinylcarbonyl)amino]-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



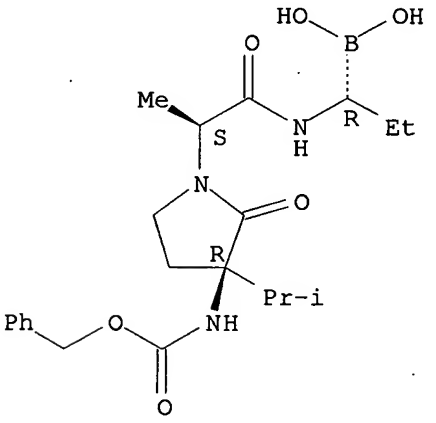
RN 779357-95-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[(1S)-2-[[(1R)-1-boronopropyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-3-(1-methylethyl)-2-oxo-3-pyrrolidinyl]-, C-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



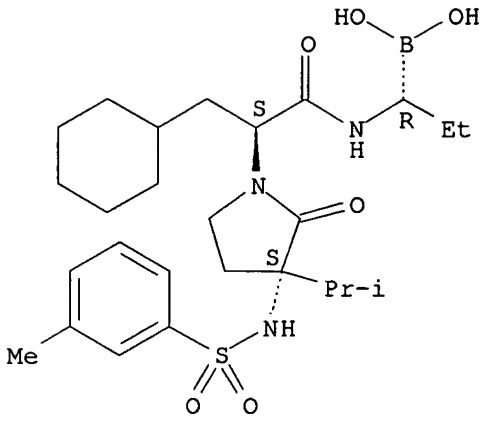
RN 779357-97-0 HCAPLUS
CN Carbamic acid, [(3R)-1-[(1S)-2-[[(1R)-1-boronopropyl]amino]-1-methyl-2-oxoethyl]-3-(1-methylethyl)-2-oxo-3-pyrrolidinyl]-, C-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **779357-83-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and in vitro characterization of lactam boronic acid based, selective, and rapidly reversible **inhibitor** of the 20S-**proteasome**)
RN 779357-83-4 HCAPLUS
CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[(3S)-3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The present invention relates to methods for inhibiting proteasome comprising administering to mammals in need thereof a compound having Formula (I).

2004:633462 Document Number 141:167752 Methods for inhibiting proteasome. Purandare, Ashok Vinayak; Laing, Naomi Mae (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2004064755 A2 20040805, 127 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1587 20040120. PRIORITY: US 2003-PV442182 20030123.

ST antitumor 26S **proteasome inhibitor** prepn
cancer therapy

IT Antitumor agents
Drug delivery systems
Mammalia
Neoplasm
(methods for inhibiting proteasome)

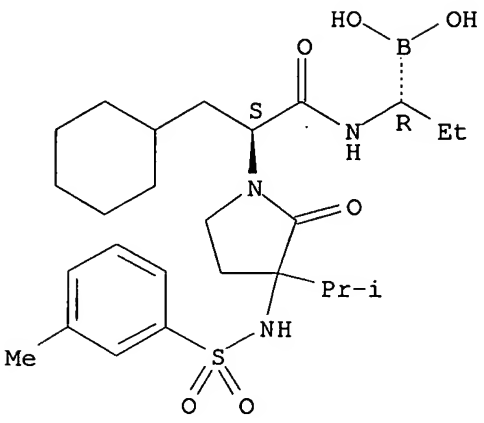
IT 323196-84-5P 323196-85-6P 323196-86-7P 323196-88-9P 323196-89-0P
323196-90-3P 323196-91-4P **323196-93-6P** 323196-96-9P
323196-97-0P 323197-00-8P 323197-01-9P 323197-02-0P 323197-03-1P
323197-06-4P 323197-07-5P 323197-08-6P 323197-09-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for inhibiting proteasome)

IT **323196-93-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for inhibiting proteasome)

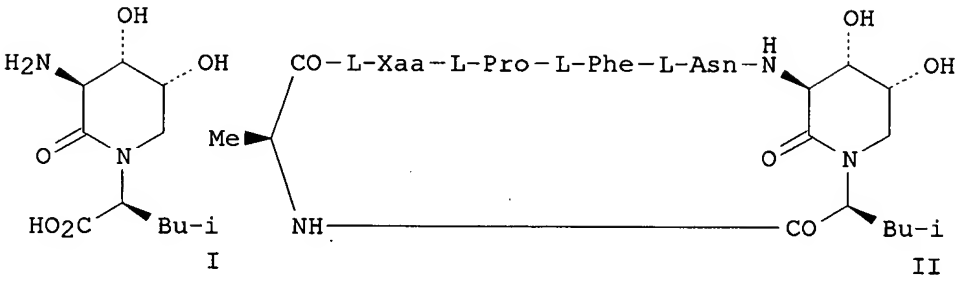
RN 323196-93-6 HCAPLUS

CN Boronic acid, [(1R)-1-[[(2S)-3-cyclohexyl-2-[3-(1-methylethyl)-3-[[(3-methylphenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]-1-oxopropyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



AB Hydroxyaminolactam I has been used as a constrained surrogate for Ser-Leu in the synthesis of analogs of the cycloheptapeptide stylostatin 1, cyclo(Pro-Phe-Asn-Ser-Leu-Ala-Ile). The rate of cyclization through formation of the Ile-Pro amide bond allowed the authors to prove that I induced a turn in the linear precursor. Ring closure at the Pro-Phe amide bond was much quicker and provided access to larger amts. of the target structures, with high purity. The conformation of ψ-stylostatin derivative II (Xaa = L-Ile) was compared to that of native stylostatin 1 using NMR anal. Inhibition of the growth of **cancer** cell lines was evaluated for II (Xaa = L-Ile, D-allo-Ile) and for epi-stylostatin, cyclo(Pro-Phe-Asn-Ser-Leu-Ala-D-allo-Ile), and the results were compared to that of the native stylostatin 1. None of the compds. showed activity below 1 μM. A possible relationship between the decrease in activity and the presence of the piperidone Ser-Leu surrogate is considered.

2003:922776 Document Number 140:111676 Constrained Derivatives of Stylostatin 1. 1. Synthesis and Biological Evaluation as Potential Anticancer Agents. Forns, Pilar; Piro, Jordi; Cuevas, Carmen; Garcia, Monica; Rubiralta,

Mario; Giralt, Ernest; Diez, Anna (Laboratori de Quimica Organica, Facultat de Farmacia, Universitat de Barcelona, Barcelona, 08028, Spain). Journal of Medicinal Chemistry, 46(26), 5825-5833 (English) 2003. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 140:111676. Publisher: American Chemical Society.

AB . . . II (Xaa = L-Ile) was compared to that of native stylostatin 1 using NMR anal. Inhibition of the growth of **cancer** cell lines was evaluated for II (Xaa = L-Ile, D-allo-Ile) and for epi-stylostatin, cyclo(Pro-Phe-Asn-Ser-Leu-Ala-D-allo-Ile), and the results were compared to. . .

IT Intestine, **neoplasm**
(colon; preparation, conformation and biol. evaluation of constrained derivs. of cyclic peptide stylostatin-1 as potential anticancer agents)

IT Antitumor agents
Conformation
Cyclization
Leukemia
Melanoma
Ovary, **neoplasm**
Pancreas, **neoplasm**
Prostate gland, **neoplasm**
(preparation, conformation and biol. evaluation of constrained derivs. of cyclic peptide stylostatin-1 as potential anticancer agents)

IT 224824-97-9P 646057-70-7P 646057-74-1P 646057-78-5P
646057-80-9P 646057-83-2P 646057-84-3P 646057-85-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, conformation and biol. evaluation of constrained derivs. of cyclic peptide stylostatin-1 as potential anticancer agents)

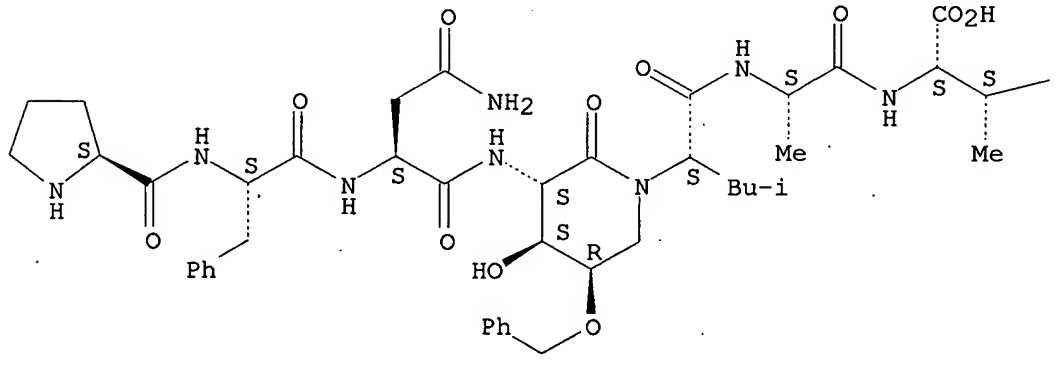
IT **646057-80-9P 646057-83-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, conformation and biol. evaluation of constrained derivs. of cyclic peptide stylostatin-1 as potential anticancer agents)

RN 646057-80-9 HCAPLUS

CN L-Isoleucine, L-prolyl-L-phenylalanyl-L-asparaginyl-(αS,3S,4S,5R)-3-amino-4-hydroxy-α-(2-methylpropyl)-2-oxo-5-(phenylmethoxy)-1-piperidineacetyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

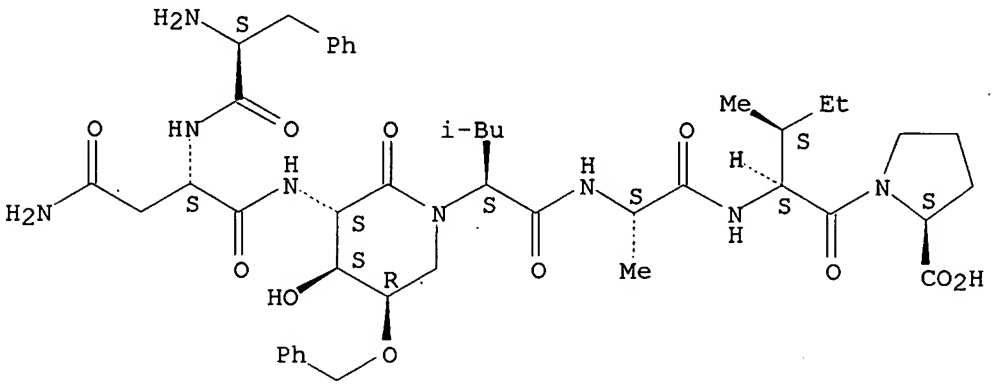
PAGE 1-A



—Et

RN 646057-83-2 HCAPLUS
CN L-Proline, L-phenylalanyl-L-asparaginyl-(αS,3S,4S,5R)-3-amino-4-hydroxy-α-(2-methylpropyl)-2-oxo-5-(phenylmethoxy)-1-piperidineacetyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Due to its role in regulating the cell cycle, Cdc25 (a family of dual specificity phosphatases) is a potential target for therapies aimed at controlling proliferative diseases, but rational, structure-based design has not been possible because of the lack of accurate 3-dimensional data. The present invention relates to polypeptides which comprises the ligand binding domain of human Cdc25 proteins, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the 3-dimensional structure of the catalytic domain of Cdc25. In particular, a high resolution crystal structure was obtained for the polypeptide denoted CDC25B(ΔN8B), comprising residues Glu-368 through Arg-562 of human Cdc25B, complexed with a pentapeptide inhibitor denoted cdc1249 (2-methoxynaphthyl-1-carboxy-(4-sulfomethyl)-L-Phe-L-Glu-L-Glu-L-naphthylalanine-L-Glu-amide). The invention also relates to the use of the 3-dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. The syntheses and structures of a large number of putative pentapeptide inhibitors are also provided. Such inhibitors have potential in the treatment of diseases associated with excessive cellular proliferation, such as **cancer**, restenosis, reocclusion of coronary artery, and inflammation.
2002:696111 Document Number 137:228607 Crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors. Taylor, Neil R.; Borhani, David; Epstein,

David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark (BASF Aktiengesellschaft, Germany; GPC Biotech Inc.). PCT Int. Appl. WO 2002070680 A1 20020912, 351 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US6587 20010301.

AB . . . inhibitors are also provided. Such inhibitors have potential in the treatment of diseases associated with excessive cellular proliferation, such as **cancer**, restenosis, reocclusion of coronary artery, and inflammation.

IT Inflammation
Neoplasm
(design of agents for treatment of; crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

IT 329277-01-2P 329277-02-3P 329277-03-4P 329277-04-5P 329277-05-6P
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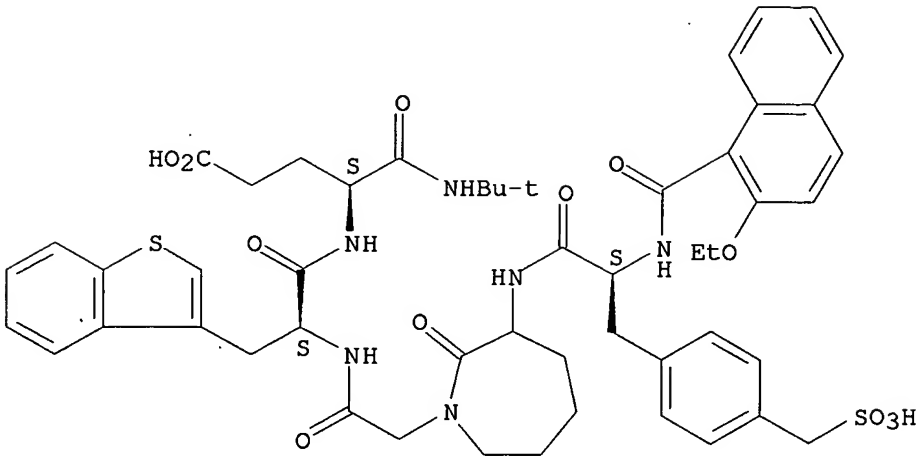
457889-78-0P 457889-79-1P 459140-70-6P 459140-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

IT **329277-28-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

RN 329277-28-3 HCAPLUS

CN L-α-Glutamine, N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-3-benzo[b]thien-3-yl-L-alanyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The present invention relates to polypeptides which comprise the ligand binding domain of CDC25, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the 3-dimensional structure of the catalytic domain of CDC25 alone and in complexes with pentapeptide inhibitors. Atomic coordinates are provided from x-ray diffraction of crystals of CDC25A and CDC25B catalytic domains in the presence and absence of various inhibitors. The invention also relates to the use of the 3-dimensional structure of the CDC25 catalytic domain in methods of designing and/or identifying potential inhibitors of CDC25 activity, for example, compds. which inhibit the binding of a native substrate to the CDC25 catalytic domain. The method comprises the steps of (1) identifying one or more functional groups capable of interacting with one or more subsites of the CDC25 catalytic domain, and (2) identifying a scaffold which presents the functional group or functional groups in a suitable orientation for interacting with one or more subsites of the CDC25 catalytic domain. Since CDC25 is a potential target for therapies aimed at controlling proliferative disease, the atomic coordinates allow rational structure-based design of potential agents for the treatment of **cancer**, restenosis, reocclusion of coronary artery, or inflammation.

2001:168124 Document Number 134:218936 Crystal structure of CDC25 proteins and its use in rational design of inhibitors. Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark (Basf Aktiengesellschaft, Germany). PCT Int. Appl. WO 2001016300 A2 20010308, 314 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO

2000-US23473 20000825. PRIORITY: US 1999-PV172215 19990831.

AB . . . therapies aimed at controlling proliferative disease, the atomic coordinates allow rational structure-based design of potential agents for the treatment of **cancer**, restenosis, reocclusion of coronary artery, or inflammation.

IT 329276-26-8P 329276-27-9P 329276-28-0P 329276-29-1P 329276-30-4P
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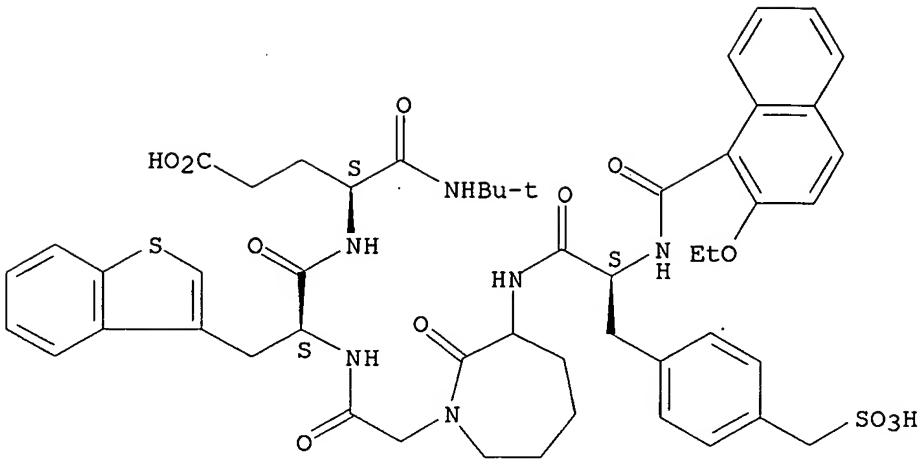
329776-39-8P 329776-40-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure of CDC25 proteins and its use in rational design of inhibitors)

IT **329277-28-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure of CDC25 proteins and its use in rational design of inhibitors)

RN 329277-28-3 HCAPLUS

CN L-α-Glutamine, N-[(2-ethoxy-1-naphthalenyl)carbonyl]-4-(sulfomethyl)-L-phenylalanyl-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-3-benzo[b]thien-3-yl-L-alanyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The authors have been interested in the design and synthesis of bombesin receptor antagonists because this class of compds. has been proposed to play a growth factor role in human small cell lung **carcinoma** systems in vitro and in vivo. These last observations suggest that bombesin or mammalian-related gastrin releasing peptides (GRP) and neuromedin B (NMB) receptor antagonists may have clin. utility as inhibitors of the physiol. response to GRP in human diseases. To decrease the peptidic character of the authors' compds. and to obtain active and constrained compds., they have synthesized analogs of the potent nonapeptide bombesin agonist H-D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-Leu-NH2 in which the dipeptide Val-Gly has been replaced by various constrained non-peptide moieties. Ability of these analogs to bind the bombesin receptor was studied. In another series and by homol. with gastrin the authors have also synthesized C-terminal Gly-extended analogs of the nonapeptide bombesin agonist. C-terminal Gly-extended peptides are biosynthetic precursors of amidated peptides. These analogs were tested for their ability to bind the bombesin receptor and to stimulate the proliferation of 3T3 cells.

2000:894783 Document Number 134:232063 Synthesis and pharmacological evaluation of a new series of bombesin analogs. Cristau, Michele; Devin, Chantal; Oiry, Catherine; Galleyrand, Jean-Claude; Pannequin, Julie; Bernad, Nicole; Fehrentz, Jean-Alain; Martinez, Jean (Laboratoire des Amino-acides, Peptides et Proteines, UMR 5810, CNRS-Universites Montpellier I et II, Montpellier, 34060/2, Fr.). Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999, Meeting Date 1999, 636-638. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth. (English) 2000. CODEN: 69ATHX.

AB . . . antagonists because this class of compds. has been proposed to play a growth factor role in human small cell lung **carcinoma** systems in vitro and in vivo. These last observations suggest that bombesin or mammalian-related gastrin releasing peptides (GRP) and neuromedin. . .

IT Lung, **neoplasm**
(small-cell **carcinoma**; bombesin analog synthesis and pharmacol. evaluation as antagonists of bombesin receptors and role in

cell proliferation)

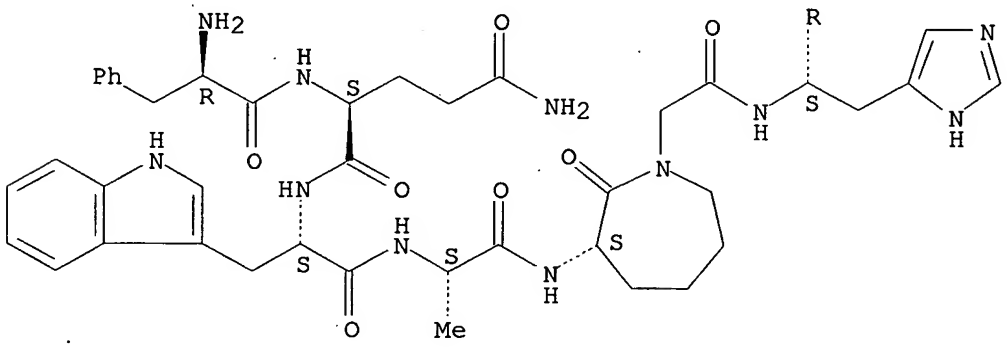
IT 138370-40-8P **285564-61-6P 285564-62-7P**
330436-08-3P 330436-09-4P 330436-10-7P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(bombesin analog synthesis and pharmacol. evaluation as antagonists of bombesin receptors and role in cell proliferation)

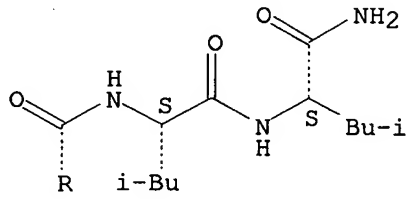
IT **285564-61-6P 285564-62-7P 330436-08-3P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(bombesin analog synthesis and pharmacol. evaluation as antagonists of bombesin receptors and role in cell proliferation)

RN 285564-61-6 HCAPLUS

CN L-Leucinamide, D-phenylalanyl-L-glutaminyl-L-tryptophyl-L-alanyl-(3S)-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





RN 285564-62-7 HCAPLUS

CN L-Leucinamide, N2-[3-(4-hydroxyphenyl)-1-oxopropyl]-L-glutaminyl-L-tryptophyl-L-alanyl-(3S)-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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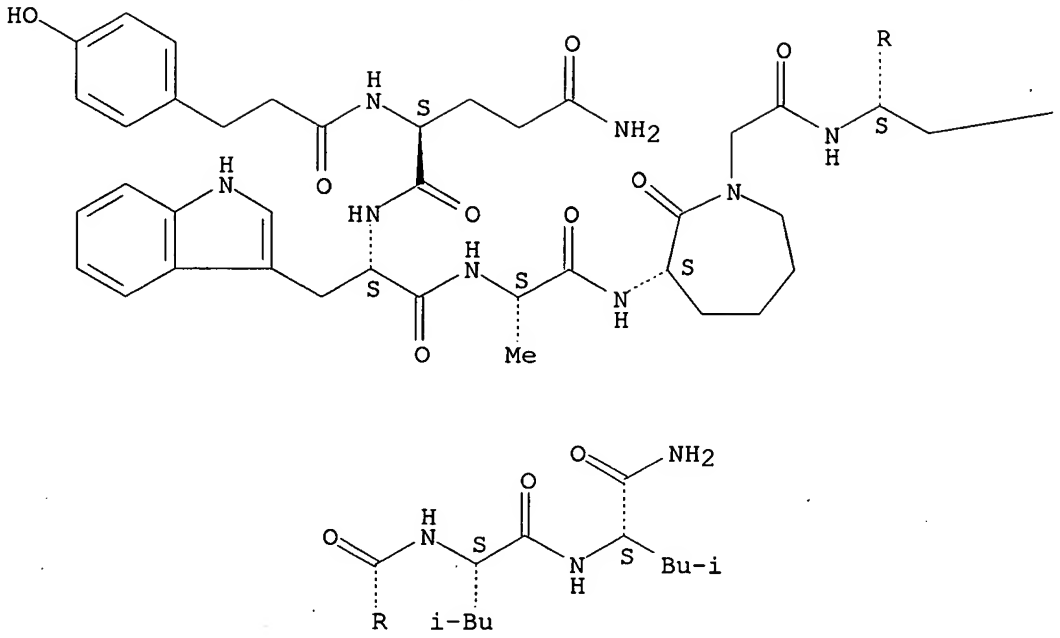

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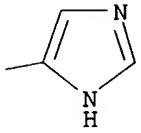

RN 330436-08-3 HCAPLUS
CN L-Histidinamide, D-phenylalanyl-L-glutaminyl-L-tryptophyl-L-alanyl-(3S)-3-aminohexahydro-2-oxo-1H-azepine-1-acetyl-N-[(1S)-2-hydroxy-1-(2-methylpropyl)heptyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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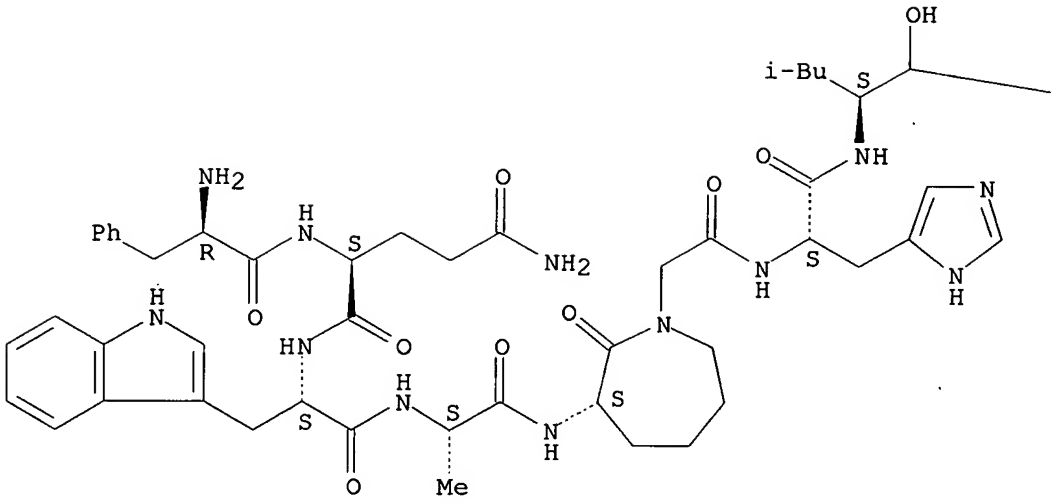

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